REMARKS

1. Response to Objections

1.1. We thank the examiner for indicating that claim 15 is allowable if rewritten in independent form, however it is our position that the base claim is allowable and hence the objection to claim 15 should be withdrawn.

1.2. In response to the maintained objection, we have amended the first reference to "TWEEN™80 detergent" to specify that it is "polyoxyethylene (20) sorbitan monooleate (CAS Registry No. 9005-65-6)", as stated in several MSDS's. We do not think it should be necessary to repeat this detailed information at every mention of "TWEEN™80 detergent".

1.3. In response to the new claim objection concerning "adaption" vs. "adaptation", we have amended claim 1 to refer to the latter.

2. Written Description Issues

2.1. The Examiner questions the basis for claim 8, "malic acid in the range of 1-50 mg/L". According to page 25, lines 2-4 of the last amendment, the basis was at P16, L27. But reviewing that passage, we see that 1-50 g/L was intended. Upon further reflection, we have decided that in view of the examples a more desirable range to recite would be 1 to 10 g/L, per L28.

2.2. The more general written description issue is whether the three deposited strains (DSM15569, DSM15570, DSM15571) are representative of the claimed genus even though the strains in question were obtained by random mutation.

As the examiner is perhaps aware, the Federal Circuit has agreed to rehear Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co. en banc (Case No. 2008-1248, August 21, 2009). See www.cafc.uscourts.gov/opinions/08-1248ebo.pdf. Specifically

the Court has agreed to consider whether (1) the patent statute in fact requires a written description requirement separate from the enablement requirement, and, (2) if so, the scope and purpose of that requirement.

We respectfully submit that in view of the relevance of this appeal to the instant case, finality should be withdrawn. (Note also our separate and independent petition for withdrawal of finality in view of errors in the restriction.) If finality is withdrawn, this amendment will be entered as of right, and we will then file a petition for six month suspension.

The Examiner has taken the position that since Applicant has not characterized the precise genetic nature of the mutations in the parental strain that characterize, Applicant should be limited to the deposited strains.

Were this view of written description to prevail, patents on novel organisms obtained by random mutation and selection, or spontaneous mutants isolated from nature, would be commercially worthless, as the protection limited to the deposited strain would be easily evaded as competitors ordered deposited strains shipped by the IDA to a location outside the USA, further mutated it there, and then used the further mutated strain in the USA with impunity[1].

Alternatively the competitors could make mutants, even in the USA, of a non-infringing parental strain, and screen (using the disclosed screening assay) for mutants with the same functionality.

Inventors and their companies would then learn to keep such organisms as trade secrets rather than enriching the art

[1] Claim 105, if allowed, does cover mutants of the deposited strains.

by depositing the organisms and describing their characteristics.

The Examiner cites Eli Lilly, Amgen and Fiddes as basis for requiring disclosure of the sequence of a nucleic acid or protein. These cases all related to claims to nucleic acids or proteins. The present claims are to organisms of a class which performs malolactic fermentation. The cases on written description do not require that "every invention must be described in the same way". The Examiner is surely aware that the PTO has been granting patents on new microorganisms since well before DNA sequencing methods were developed, and hence before there was knowledge of the specific sequence-activity correlations.

The Examiner says at page 7, lines 11-25:

> While the cited cases are directly related to nucleic acids and proteins, the legal principles discussed are not limited to nucleic acids and proteins. Furthermore, while applicant is claiming an organism, the fact is that the claimed characteristics of said organism are obtained through mutation of known organisms. Applicant is taking known and disclosed bacteria and altering their nucleic acids so that said bacteria will have new characteristics. It is the structure of these nucleic acids that leads to the claimed functions. Therefore, the principles discussed in the cited cases are relevant to the instant case. With the exception of the deposited organisms, which are described not by any structural information, but rather only by virtue of the biological deposit, applicant has described their invention using functional characteristics alone. These characteristics have not been correlated in any way to any known structure.

We agree that the metabolic characteristics of the deposited organisms are the result of mutation of the genes of those organisms. However, it does not follow that a claim to

a mutated organism is subject to the WD standard which Eli Lilly developed for claims to nucleic acids.

In Fiers, cited by the examiner, the court emphasized not merely that the count was to a product, but that it was a chemical, and it characterized DNA as being a complex chemical. But an organism is not merely a chemical.

Also, the disclosure is of more than merely a desired function for applicants' organisms. Applicant deposited three different strains (P42) that had the desired function (see examples 2-4 for DSM15571; example 4 for DSM15569 and 15570; also example 6 for 15569). In Enzo Biochem., Inc. v. Gen Probe Incorporated, 323 F.3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002), on rehearing, the court held that the deposited *Neisseria gonorrhoeae* inherently described the claimed probes because the inserts could have been recovered and sequenced. Like the patentees in Enzo, we had strain deposit information in the application as filed, see e.g., P46, L24-32. The art could compare the differences between the genomes of DSM15569, 15570, and 15571 on the one hand, and the reference strain DSM2007 on the other.

Moreover, the PTO has failed to make a showing that it is rare for a radiation- or chemically-induced mutant of Oenococcus oeni to possess the claimed trait of reduced citric acid-degradative activity. It may be that applicants merely were the first to recognize that such mutants could be made, and to provide an assay for identifying them.

If mutations conferring such functionality are not rare, within the taxon of interest, it follows that the three disclosed mutants are representative of the broader patent genus, at the very least of the species *Oenococcus oeni* (claim 2), and arguably of the biological genus *Oenococcus* (claim

105), or the "supergenus" comprising *Oenococcus* and the related genera *Lactobacillus* and *Pediococcus* (claim 1).

3. Miscellaneous

3.1. In the January 7, 2009 office action, bottom of page 6, the examiner questioned whether it might be possible (1) for the contemplated organism to degrade all of the citric acid if the amount of citric acid in the medium was very low, and (2) for organisms other than those contemplated to degrade less than 80% of the citric acid if the amount contemplated was very high.

A similar question was raised, top of page 7, concerning the malic acid limitation of claim 8.

In response, we required that in the citric acid degradation test contemplated by claim 1, the citric acid level was in the range of 1-5000 mg/ml, and in the malic acid degradation test of claim 8, that the malic acid level be in the range of 1-50 mg/L (sic, 1-50g/L intended).

However, it has occurred to us that it might still be possible to manipulate the inoculation cell density or the period of time over which degradation is observed so as to defeat the intent of the claims. Hence, we have reviewed the best parameters.

In Example 3, $2x10^6$ CFU/ml of our strain DSM15571 was inoculated into 4L of the medium (wine). The levels of malic acid and citric acid were 3300 mg/L and 450 mg/L, respectively (see Example 2, P43, L27; cp. Fig. 4 ordinates). As shown in Fig. 4, this strain degraded the malic acid, essentially exhausting it after 10 days (cp. P46, L15), and in the same period levels of citric acid remained essentially constant (cp. P46, L15-16).

In Example 4, strains DSM15569, DSM15570 and DSM15571 were compared with the commercial culture DSM7008 having a normal citric acid metabolism, with the same inoculation concentration as in example 2 (i.e, $5x10^6$ CFu/ml, per P45, L18) but at a larger scale (250L).

It appears that malic acid levels exceeded 1000mg/L and citric acid levels were in the range 300-400mg/L. (Fig. 5 ordinates). Initial microbial levels were in the $1x10^6$ to $1x10^7$ range. All barrels completed the malic acid degradation within 19-24 days (P47, L1-2) and indeed Fig. 5 appears to show completion within 20 days. It does not appear that the mutant strains degraded the citric acid (P47, L2-3), whereas it can be seen that the reference strain reduced citric acid levels to the 0-100 mg/L range over the same period. If the initial level was 330 mg/L, and the final level 50 mg/L, (both estimated by Counsel by eye), that would be a reference strain reduction of 280/330, i.e., 84.8% degradation, and thus distinguished by original claim 1.

A similar comparison appears in Fig. 6A. Here malic acid levels declined from about 1750mg/L (estimated) to zero (estimated) in 25 days, whereas the citric acid levels were steady at slightly over 300 mg/L for mutant strains, and declined to zero (100% degradation) for the reference strain. And, in Fig. 6B, malic acid levels declined from over 3000mg/L in 5-15 days, but the mutant strains failed to degrade citric acid at levels of about 500mg/L. Two reference strains were tested, which completely degraded the citric acid in 13 and 20 days, respectively.

Beyond what is in the examples, there is relevant disclosure in the description as to:

(1) the maximum percentage of citric acid degraded (P14, L17-25)

(2) the maximum percentage degraded within a particular time period relative to the initiation of fermentation (P14, L25-P15, L2), such as within 10 days (P14, L29)

(3) the maximum percentage degraded within a particular time period defined relative to the completion of the malolactic fermentation (P15, L4-13)

(4) the maximum percentage degraded while the organism is metabolically active (P15, L18-21)

(5) the minimum percentage of malic acid degraded (P15, L22-27)

(6) the minimum percentage of malic acid degraded to lactic acid (P15, L29-32)

(7) the time period for completion of the malolactic acid degradation (P16, L5-7)

(8) the initial PH (P16, L11-14)

(9) the initial ethanol content (P16, L15-21)

(10) the initial sugar content (P16, L22-26)

(11) the initial malic acid content (P16, L27-30)

(12) the initial citric acid content (P16, L31-35)

(13) the temperature (P17, L2-4)

(14) the initial microbial inoculation concentration (P17, L6-10)

(15) minimum malic acid degradation under specified conditions (P17, L12-20)

(16) maximum citric acid degradation under specified conditions (P17, L22-31).

In view of the foregoing, we have deemed it appropriate to amend the citric acid degradation test contemplated by claim 1 to make it more specific as to the test conditions.

In particular, we now recite

--degradation of citric acid is not more than 50%, rather than 80%

--degradation of citric acid is determined as of the essential completion of the malolactic fermentation (Figs. 4, 5, 6A, 6B), i.e., which in accordance with P15, L13-16 we consider to be when the malic acid level is reduced to 30 mg/L.

--initial citric acid concentration is 100-1000 mg/L (P22, L27 and 30) (this includes the values shown in Figs. 4-6)

--initial malic acid concentration is 1000-10,000 mg/L (1-10g/L) (P19, L32)

--initial microbial concentration is $1x10^6$-$5x10^7$ CFu/ml (P17, L9-10).

Similar amendments have been made to claim 8.

Several new claims are presented:

104: organism is Oenococcoccus. Basis at P19, L31.

105: organism is DSM15569, 15570 or 15571, or a mutant derived therefrom. Basis at P19, L32-34 in conjunction with P26, L28 to P27, L23.

106: organism obtainable by recited method; the method is that of steps (i)-(iii) of original claim 55.

107: organism obtained by recited method; the method (1) is based on steps (i)-(iii) of claim 50, and the method (2) uses organisms selected by (1) as the starting point for further mutation.

108: see claim 104.

109: see P26, L31.

110: see P27, L7 and P42, L18-19.

3.2. In the Petition Against Restriction filed October 15, 2009, section 3, we said that we would shortly file an amendment cancelling "activation solution" claims 63-66 and 68-73. However, on closer inspection of claim 63, we realized

that it referred to a "microbial organism" in clause (iii) and hence could be amended to depend from claim 1. Hence, we have retained claims 63-66, 68 and 70-73, cancelling 69 because it recited only organisms not within the scope of claim 1.

Respectfully submitted,

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